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19. KEY WORDS (Continue on reverse side if necessary and identify by block number) <i>yield</i>	20. ABSTRACT (Continue on reverse side if necessary and identify by block number) The action of n-butyllithium in hexane on $\text{CF}_3\text{BrCH}=\text{CH}_2/\text{CF}_2=\text{CH}-\text{CH}_2\text{Br}$ (5:2 + 20:1 mixture) in 5:1:1 THF/ $\text{Et}_2\text{O}$ /pentane at $-95^\circ\text{C}$ generates gem-difluoroallyllithium which may be trapped, generally in good yield, by the <i>in situ</i> procedure using triorganochlorosilanes ( $\text{+ R}_3\text{SiCF}_2\text{CH}=\text{CH}_2$ ) and aldehydes and ketones ( $\text{+ RR}'\text{C}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$ ).	

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GEM-DIFLUOROALLYLLITHIUM: IMPROVED SYNTHESIS

BRINGS IMPROVED APPLICABILITY

by

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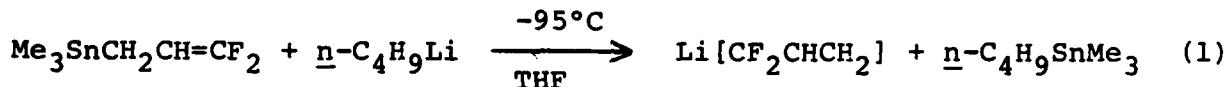
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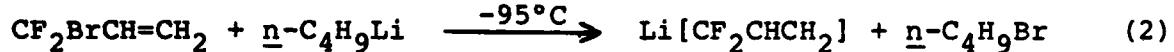
gem-Difluoroallyllithium, I, is of interest as a reagent which allows the introduction of a functional fluorinated substituent into organic and organometallic compounds. We have generated this reagent at low temperature by the transmetalation procedure (eq. 1).<sup>1</sup> The reagent is not stable in solution even at



-95°C and cannot be preformed prior to its reaction with the desired substrate. Its reactions with chlorosilanes were carried out by the in situ procedure: slow addition of n-C<sub>4</sub>H<sub>9</sub>Li solution to a mixture of Me<sub>3</sub>SnCH<sub>2</sub>CH=CF<sub>2</sub> and the chlorosilane, so that the reagent is trapped as it is formed. The addition of Li[CF<sub>2</sub>CHCH<sub>2</sub>] to the C=O of 3-pentanone by the in situ procedure was not successful since the rate of n-butyllithium addition to the ketone is faster than its rate of displacement of the difluoroallyl substituent from tin. Addition of Li[CF<sub>2</sub>CHCH<sub>2</sub>] to the C=O bond of 3-pentanone to give (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>-C(OH)CF<sub>2</sub>CH=CH<sub>2</sub> (75% yield) was achieved by the method of alternate, incremental additions.<sup>1</sup> However, this procedure is tedious and cumbersome and not well adapted to larger scale application.

In view of these difficulties with Li[CF<sub>2</sub>CHCH<sub>2</sub>]/carbonyl reactions and also because of the difficult, multi-step preparative route to Me<sub>3</sub>SnCH<sub>2</sub>CH=CF<sub>2</sub>, the Li[CF<sub>2</sub>CHCH<sub>2</sub>] precursor,<sup>1</sup> we sought an alternative method of generating gem-difluoroallyllithium.

The benzoyl peroxide-induced addition of dibromodifluoromethane to ethylene in an autoclave at 80°C was reported by Tarrant and Lovelace<sup>2</sup> to give  $\text{CF}_2\text{BrCH}_2\text{CH}_2\text{Br}$ . The single example of this reaction which was described<sup>2</sup> involved a runaway exotherm with consequent loss of most of the contents of the autoclave through the rupture disk, but we have used this reaction repeatedly without mishap. In a typical example, the yield of  $\text{CF}_2\text{BrCH}_2\text{CH}_2\text{Br}$  was 76%, based on unrecovered  $\text{CF}_2\text{Br}_2$ , which had been used in excess. Treatment of  $\text{CF}_2\text{BrCH}_2\text{CH}_2\text{Br}$  with aqueous KOH at 95-98°C gave a 5:2 mixture (by NMR) of  $\text{CF}_2\text{BrCH=CH}_2$  and  $\text{CF}_2=\text{CHCH}_2\text{Br}$  in 74% yield. Slow distillation of this product mixture gave a distillate with an isomer ratio which had been increased to ca. 20:1. Either isomer mixture serves well as a precursor for gem-difluoroallyllithium (eq. 2)<sup>3</sup>. In situ



reactions with chlorosilanes gave moderate-to-good yields of 1,1-difluoroallylsilanes. In one such reaction, when 15 mmol of n-butyllithium in hexane was added slowly to a mixture of 19 mmol of 20:1  $\text{CF}_2\text{BrCH=CH}_2/\text{CF}_2=\text{CHCH}_2\text{Br}$  and 30 mmol of  $\text{PhMe}_2\text{SiCl}$  in 5:1:1 (by volume) THF/Et<sub>2</sub>O/pentane at -95°C (under nitrogen, with stirring for 60 min. at -95°C),  $\text{PhMe}_2\text{SiCF}_2\text{CH=CH}_2$ <sup>1</sup> was produced in 71% yield. Also prepared in this manner were  $\text{Et}_3\text{SiCF}_2\text{CH=CH}_2$  (51%), n-Pr<sub>3</sub>Si-CF<sub>2</sub>CH=CH<sub>2</sub> (50%) and Me<sub>3</sub>SiCF<sub>2</sub>CH=CH<sub>2</sub> (89%). In the case of the latter, separation from the n-butyl bromide formed in the Li/Br exchange reaction could not be effected by distillation. However, ethyllithium may be used in place of n-butyllithium to form  $\text{Li}[\text{CF}_2\text{CHCH}_2]$  and the ethyl bromide formed in the exchange is much more volatile and does

not interfere in product isolation.

The real utility of this new procedure for  $\text{Li}[\text{CF}_2\text{CHCH}_2]$  lies in its applicability to aldehyde and ketone difluoroallylation. In the  $\text{Me}_3\text{SnCH}_2\text{CH}=\text{CF}_2/\underline{n\text{-C}_4\text{H}_9}\text{Li}$  route to  $\text{Li}[\text{CF}_2\text{CHCH}_2]$  it is a matter of nucleophilic displacement of  $[\text{CF}_2\text{CHCH}_2]^-$  from tin by  $\underline{n\text{-butyl-}}$  lithium. This polar process is relatively slow at low temperature and cannot compete with the more rapid addition of the lithium reagent to the  $\text{C=O}$  bond. On the other hand, the lithium/halogen exchange reaction, especially when polyhalomethanes are involved, is an electron-transfer process<sup>4</sup>, and, as such, is rapid even at low temperature in ether solvents. Therefore, one might expect that the  $\text{CF}_2\text{BrCH}=\text{CH}_2/\underline{n\text{-C}_4\text{H}_9}\text{Li}$  reaction would proceed at a rate comparable to, or even faster than,  $\underline{n\text{-butyllithium}}$  addition to the carbonyl compound. Such was found to be the case. In situ reactions in which  $\text{CF}_2\text{Br}-\text{CH}=\text{CH}_2/\text{CF}_2=\text{CHCH}_2\text{Br}$  and the aldehyde or ketone in 5:1:1 THF/Et<sub>2</sub>O/pentane solvent at -95°C (under nitrogen, with stirring for 90 min.), with subsequent slow warming to room temperature and hydrolysis, gave alcohols of type  $\text{RR}'\text{C}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$  in good yield (by GLC). Thus prepared were  $\text{Me}_2\text{C}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$  (41%),  $\text{Et}_2\text{C}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$  (70%), cyclo- $\text{C}_6\text{H}_{10}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$  (59%),  $\text{PhMeC}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$  (73%),  $\underline{n\text{-C}_4\text{H}_9}\text{CH}(\text{OH})-\text{CF}_2\text{CH}=\text{CH}_2$  (87%) and  $\text{Me}_3\text{CCH}(\text{OH})\text{CF}_2\text{CH}=\text{CH}_2$  (95%).<sup>5</sup>

One object of our study of the reactions of gem-difluoroallyl-lithium with carbonyl compounds was to see if its  $\alpha/\gamma$  regiosel ectivity in  $\text{C=O}$  additions was the same as or different from that of gem-dichloroallyllithium, a reagent which we had prepared and investigated in an earlier study.<sup>6</sup> As in the case of  $\text{Li}[\text{CCl}_2\text{CHCH}_2]$ , the reactions of gem-difluoroallyllithium with aliphatic ketones resulted in C-C bond formation at the halogenated terminus of the re-

agent. However, in contrast to the results obtained in reactions of gem-dichloroallyllithium with aliphatic aldehydes and with aceto-phenone (mixtures of alcohols,  $RR'C(OH)CCl_2CH=CH_2$  and  $RR'C(OH)CH_2CH=CCl_2$ , in which the former predominated), such reactions of gem-difluoroallyl-lithium gave only a single product of type  $RR'C(OH)CF_2CH=CH_2$ . Further work will be aimed at a more detailed comparison of the reactions of  $Li[CF_2CHCH_2]$  and  $Li[CCl_2CHCH_2]$  using a wider selection of carbonyl substrates.

The  $Me_3SnCH_2CH=CF_2/n-C_4H_9Li$  in situ procedure for gem-difluoro-allyllithium also failed to give the desired result in the attempted difluoroallylation of dimethyldichlorosilane to  $Me_2Si(CF_2CH=CH_2)_2$ . Apparently the substitution of the first chlorine by n-butyllithium is faster than its transmetalation with the tin precursor, and  $Me_2(n-C_4H_9)SiCF_2CH=CH_2$  was the product which was isolated.<sup>1</sup> In contrast, the rate of the  $CF_2BrCH=CH_2/n-C_4H_9Li$  reaction is faster than that of n-butyllithium with dimethyldichlorosilane under the conditions of our experiment, and  $Me_2Si(CF_2CH=CH_2)_2$  was obtained in moderate yield.

Using this new and improved route for its generation, we are investigating further aspects of the chemistry of gem-difluoroallyl-lithium.

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